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Brief Clinical Report

Nasal Dimple as Part of the 22q11.2 Deletion Syndrome

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The phenotype of the 22q11.2 microdeletion syndrome is quite variable. We describe 2 patients with a 22q11.2 deletion and a dimpled nasal tip, which, we suggest can be the extreme of the broad or bulbous nose commonly found in the 22q11.2 deletion syndrome, and should not be confused with the more severe nasal abnormalities seen in frontonasal dysplasia. Am. J. Med. Genet. 69:290–292, 1997. © 1997 Wiley-Liss, Inc.

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PATIENT 1

A caucasian female was born vaginally at term to a 23-year-old primigravida and a 25-year-old nonconsanguinous father. The pregnancy was complicated by light bleeding in the first trimester and elevated maternal blood pressure at 33 weeks of gestation. Birth weight was 2.76 kg (10–25th centile); length 47 cm (10–25th centile); OFC 33 cm (25–50th centile). At 8 days the infant was found to have a broad nose with some lateral build-up and a dimple in the nasal tip (Fig. 1), a nevus flammeus over the left upper eyelid, an inner canthal distance of 2.5 cm, outer canthal distance of 6 cm, and interpupillary distance of 4 cm (50th centile). Ears appeared "squared off" with overfolded helices. The mouth was well formed and the palate grossly intact. A 2/6 systolic heart murmur and an umbilical hernia were present. Female external genitalia had a cleft appearance of the anterior labia majora. The limbs and dermatoglyphics were normal.

Echocardiography showed a tetralogy of Fallot (TOF). Chromosomal studies demonstrated a 46,XX karyotype. Because of the association of 22q11.2 microdeletions with conotruncal cardiac malformations [Goldmuntz et al., 1993], FISH analysis with the N25 probe (ONCOR) was performed. The patient was found to have a 22q11.2 microdeletion.

The patient's mother is in good health, however she did not speak clearly until age 3 and continues to have hypernasal speech. She also has a history of a repaired umbilical hernia, mitral valve prolapse, and bilateral placement of myringotomy tubes. Deletion studies demonstrated a maternal 22q11.2 deletion. The patient's maternal grandmother is in good health and does not have a 22q11.2 deletion by FISH. She had one spontaneous abortion at 8 weeks gestation and 4 term deliveries. The patient's maternal grandfather died at age 40 years of pancreatic cancer; he had previously been healthy. The patient's maternal uncle had a daughter with aortic stenosis. Deletion studies have not yet been performed in these family members.

PATIENT 2

This young man presented at age 18 years for correction of his broad, bifid nasal tip. At this time he was found to have a submucous cleft palate, bifid uvula and velopharyngeal incompetence. Neonatally he had hypocalcemia, atrial septal defect and delayed development. At 28 years he was evaluated by a neurologist for dysmetria and bradykinesia caused by cerebellar atrophy [Lynch et al., 1995]. His height was 185 cm (90th centile), OFC was 57.5 cm (75–90th centile). Eyes were deep set, inner canthal distance was 3 cm, outer canthal distance was 9.5 cm and inter pupillary distance was 5.8 cm (75–90th centile). He had a prominent nasal root with a bulbous, dimpled tip, and prominent ears with thick, overfolded helices (Fig. 2). His speech was dysarthric and his gait wide based. Because of the cleft

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Fig. 1. Patient 1 at age 5 weeks; note broad nose with bifid tip.

palate, developmental delay, neonatal hypocalcemia and the facial anomalies the diagnosis of velo-cardio-facial syndrome (VCFS) was suspected. Cytogenetic and FISH analysis demonstrated an interstitial deletion of chromosome 22q11.2.

DISCUSSION

The 22q11.2 microdeletion syndrome can present as DiGeorge syndrome [Driscoll et al., 1992a; Wilson et al., 1992], as VCFS [Driscoll et al., 1992b; Kelly et al., 1993], and as conotruncal anomaly face syndrome [Burn et al., 1993]. These syndromes share characteristic facial findings including broad nasal root and prominent nasal tip, hypertelorism, small mouth, and posteriorly angulated, prominent ears with a thickened helix. Congenital conotruncal cardiac defects, cleft palate, and thymic and parathyroid hypoplasia or aplasia can also occur in these conditions. Due to the great variability of findings in affected patients a high index of suspicion is frequently required to make the diagnosis, as is demonstrated by the fact that some patients are identified only after a close relative was found to have the deletion. The presence of multiple, including subtle facial, anomalies can be helpful in diagnosing patients in a timely fashion.

We suggest that the occurrence of a nasal dimple in our two patients with 22q11.2 deletion is not coincidental. The dimpled appearance of the nasal tip probably represents the extreme of the broad and bulbous tip usually seen in this syndrome (see published photographs of case 4 and case 14 in Jedele et al., 1992; mother of family 1 in De Silva et al., 1995). It should not be confused with the bifid nose in frontonasal dysplasia [Sedano et al., 1970].

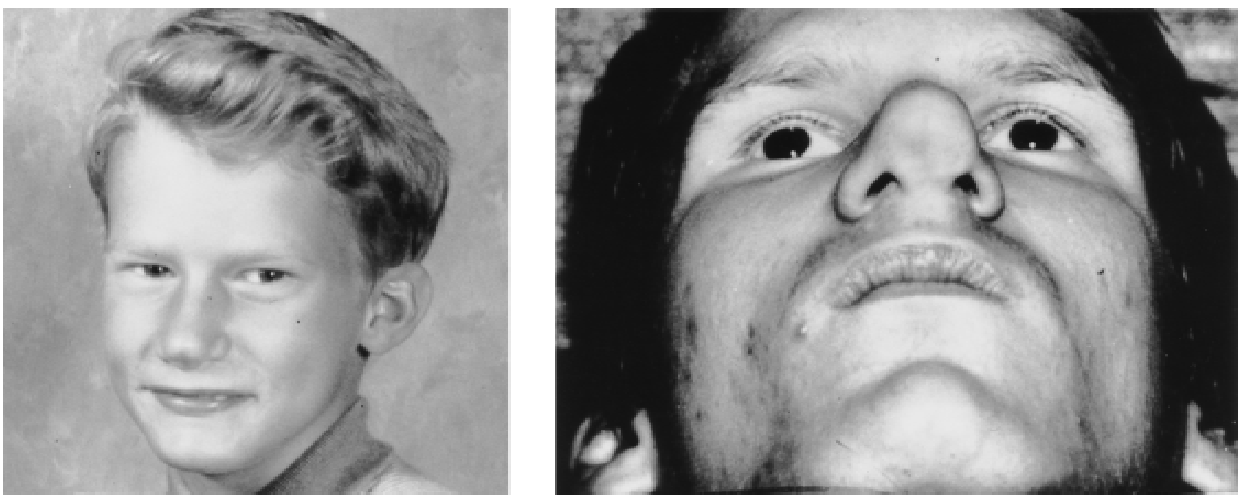

Fig. 2. Patient 2 at age 10 years (left) and at age 18 years (right); note broad, bifid nasal tip and protruding ears.

De Moor et al. [1987] reported 3 patients with TOF, frontonasal dysplasia and medial nasal grooves, similar in appearance to those of our patients. Their growth was below the 3rd centile, a more significant growth failure than expected for their cardiac condition and not typical for frontonasal dysplasia. One of them had facial findings seen in the 22q11.2 deletion syndrome, including a very broad nasal root with hypoplastic alae nasi and, as evident in the published photograph, protruding ears. We wondered if this patient might have a 22q11.2 deletion, but unfortunately he was unavailable for further studies.

In summary, we suggest that the finding of a dimpled nasal tip, in combination with other anomalies, may be consistent with the diagnosis of 22q11.2 deletion syndrome.

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